

Application No.:10/597,813

Docket No.: JCLA21512-R

**REMARKS****Present Status of the Application**

The Office Action dated April 01, 2009 objected the specification for containing sequence disclosures as set for in 37 C.F.R. 1.821(a)(1) and (a)(2). Claims 19-25 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite. Claims 19-25 were rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process. Claims 19-25 were rejected under 35 U.S.C. 102(b) as being anticipated by Murray et al. (WO 03/000656 A2).

Claims 19-21 and 23 have been amended for clarification purposes or correcting informalities. The specification has been amended for incorporating SEQ ID NOs for clarification purposes and complying with the nucleotide sequence disclosure requirements. It is believed that the amendments are supported by the original specification and drawings of this application and can overcome the objections. After entering the amendments and considering the following discussions, a notice of allowance is respectfully solicited.

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**Discussion for the objections**

The specification was objected for containing sequence disclosures as set forth in 37 C.F.R. 1.821(a)(1) and (a)(2).

The specification has been amended by assigning SEQ ID NOs. to the sequences recited in page 13, 1<sup>st</sup> paragraph to page 14, 1<sup>st</sup> paragraph of the specification of the present application.

Regarding the sequences recited in page 13 of the specification of the present application, nucleotide sequences comprising four or more than four nucleotides have been assigned with a SEQ ID NO. respectively. According to the previous Office Action, nucleotide sequences comprising less than four nucleotides are not assigned with a SEQ ID NO..

Please find enclosed a new Sequence Listing in both computer readable form (CRF) and paper copy. Applicant confirms that the paper and electronic versions of the newly submitted Sequence Listing are identical. The new Sequence Listing incorporates sequences of SEQ ID NOs. 101 to 163 and additionally including sequences 97 to 100 which were assigned to sequences of pages 17 & 19 of the present application in response to the previous Office Action.

Entry of the amendments to the specification is respectfully requested.

Withdrawal of these objections is earnestly requested.

**Discussion of 101 and 112 rejections**

Claims 19-25 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite.

Claims 19-25 were rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process.

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According to the Examiner, these rejections can be obviated by claiming "A method of" or "A process of", for example.

Claims 19-21 and 23 have been amended, while claims 22 and 24-25 have been cancelled.

Moreover, claim 19 has been amended as "A method of promoting successful regeneration and functional reconnection of damaged neural pathways in a mammal, comprising administering .... at least one said oligonucleotide ....", and claims 20-21 and 23 have been amended accordingly for clarification.

Withdrawal and reconsideration of these 112 rejections are respectfully requested.

**Discussion of Rejections under 35 U.S.C 102**

Claims 19-25 were rejected under 35 U.S.C. 102(b) as being anticipated by Murray et al. (WO 03/000656 A2; hereinafter Murray).

Claims 19, 20-21 and 23 have been amended to provide more descriptions for clarification purposes and for correcting informalities. Claims 22 and 24-25 have been cancelled.

Claim 19 has been amended as "A method of promoting successful regeneration and functional reconnection of damaged neural pathways in a mammal, comprising administering .... at least one said oligonucleotide ....".

Murray merely teaches using TGF- $\beta$ RII antisense oligonucleotides for treatment of diseases that are associated with TGF- $\beta$ RII expression.

The present application as presented by the amended set of claims discloses a method for promoting regeneration and functional reconnection of damaged neural pathways by

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administering TGF- $\beta$ RII antisense oligonucleotides. That means the method of the present application utilizes antisense oligonucleotides to prevent and treat disorders of the Central Nervous System and neuronal stem cell renewal. The TGF- $\beta$ RII antisense oligonucleotides of the present application may include the TGF- $\beta$ RII antisense oligonucleotides mentioned in the reference Murray. But the method of the present application uses the antisense oligonucleotides for promoting regeneration and functional reconnection of damaged neural pathways while Murray focuses on the treatment of cancerous diseases and diseases that involve the activation of the immune system. Moreover, a method for prevention or treatment of disorders of the Central Nervous System and neuronal stem cell renewal by administering TGF- $\beta$ RII antisense oligonucleotides is nowhere mentioned in the reference Murray. Therefore the method as recited in the amended claims of the present application is not anticipated by and being novel over the reference Murray.

In addition, Examples 6, 7 and 8 of the present application demonstrate that the method of administrating the antisense oligonucleotides successfully prevents and treats the induced inhibition of neural stem and precursor cell proliferation in cultured neural stem and precursor cells and in living animals. Furthermore, the Examples of the present application show that the claimed methods comprising administrating antisense oligonucleotide have a real curative effect on neural cells in cell culture as well as in an animal model. Thus the method recited in amended claim 19 of the present application has been shown to have a surprising advantageous effect of activity in central nervous system cells.

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Murray neither teaches nor suggests that its TGF- $\beta$ RII antisense oligonucleotides might be useful in treatment of neuronal disorders. In fact, Murray does not show that the effect of the antisense oligonucleotides to reduce expression of TGF- $\beta$ RII is connected to a real curative effect. Thus the curative effect on neural cells in cell culture as well as in an animal model of the antisense oligonucleotides of the present application would not be anticipated or expected based on the disclosures of Murray.

Clearly, Murray's disclosures not only fail to the method of promoting regeneration and functional reconnection of damaged neural pathways with the antisense oligonucleotides as claimed in the present application, but also fail to enlighten one ordinary artisan with the curative effect on neural cells in cell culture as well as in an animal model of the present application.

Accordingly, as discussed above, Murray fails to disclose each and every feature as recited in independent claim 19, and independent claim 19 patently defines over the reference Murray. Claims 20-21 and 23 depending from claim 19 therefore are not anticipated by Murray for the reasons noted above, as well as for the additional features recited therein.

Reconsideration and withdrawal of above 102 rejections are respectfully requested.

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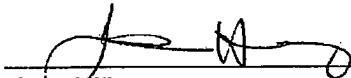
**CONCLUSION**

For at least the foregoing reasons, it is believed that the pending claims of the present application patently defines over the prior art and are in proper condition for allowance. If the Examiner believes that a telephone conference would expedite the examination of the above-identified patent application, the Examiner is invited to call the undersigned.

Respectfully submitted,  
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